the amendments can be found throughout the Specification. Support for new claims 31 and 32 can be found on page 10, lines 21-25.

Restriction Requirement

On October 1, 2001, the Examiner issued a restriction consisting of four groups: Group I: Claims 1-4 and 12-18 drawn to peptides and cultures comprising the peptides; Group II: Claims 5-11, 19, and 30 drawn to peptide libraries; Group III: Claims 20-25 drawn to methods of enhancing/inhibiting protein production; and Group IV: Claims 26-29 drawn to recombinant methods of making peptides and required the Applicants to elect a group , peptide length and sequence for examination. Applicants elected Group I without traverse. In a supplemental response, Applicants made a species election of pentapeptides and SEQ ID NO: 16. In an Official Action dated April 8, 2002, the Examiner issued a Revised Election/Restriction requirement requiring Applicants to elect one of four groups for examination, a species of peptide length and a sequence. The peptide length, sequence number and four groups were the same as the first Restriction Requirement: Group I: claims 1-4 and 12-18 drawn to peptides and cultures comprising the peptides; Group II: claims 5-11, 19, and 30 drawn to peptide libraries; Group III: claims 20-25 drawn to methods of enhancing/inhibiting protein production; and Group IV: claims 26-29 drawn to recombinant methods of making peptides. Applicants again elected Group I, the pentapeptide and sequence number 16 for examination and withdrew claims 5-11 and 19-30 from consideration. In an action on the merits dated August 28, 2002, the Examiner again revised the restriction, indicating that "[t]he claims drawn to a cell or tissue culture i.e.,

claims 4, 15-19 would not be included in Group I. These claims are distinct and different from the compounds of Group I since the claims are drawn to a different statutory subject matter, cell or tissue culture. The peptides of Group I can be made by other methods such as chemical synthesis rather than by the cell culture method of e.g., claim 4." (See Official Action at page 2.) Applicants respectfully traverse this revised restriction.

The Examiner has withdrawn claims 4, and 15-19 from Group I. Applicants submit that claims 4, and 15-19 should be recombined with Group I since the cell culture medium contains the peptides of claim 1. The Examiner will perform a search of the peptides of claim 1, therefore a search for the use of the peptides in cell culture medium will not be unduly burdensome. Reconsideration of the restriction is respectfully requested. If the Examiner does not recombine claims 4, and 15-19 with Group I, Applicants request that claim 4 be placed with Group I, and claims 15-19 be placed with Group II since the claims and the groups are drawn to the peptide and a peptide library, respectively. Finally, if the Examiner does not recombine the claims with any group, he should indicate the group into which the claims will be included. Currently, the claims have been withdrawn but not placed in a group.

REJECTIONS

Rejection of Claims 2-3 and 13-14 under, 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 2-3 and 13-14 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states, "It is not clear as to how these

claims further limit the compound claims 1 and 12. Furthermore, it is not clear as to the nucleic acid sequence that encodes the peptide. This provides confusion since two compounds are claimed i.e., nucleic acid which functions by encoding the claimed peptide of the basis claim and the peptide." Applicants respectfully traverse this rejection.

As explained in the Specification at page 3, lines 32-34 and again at page 5, lines 1-5, peptides may be produced either chemically or recombinantly. Claim 2 further limits claim 1 by specifying that the peptide is produced recombinantly. Claim 3 further limits claim 2 by specifying that the recombinant nucleic acid sequence may express the peptide as a concatemer that is cleaved to provide the peptide. Further, peptides are fragments of a protein, which are produced from nucleic acids. Due to the degeneracy the genetic code, there is usually more than one codon for any given amino acid. As such, there may be more than one nucleic acid sequence that provides the claimed peptide. This is understood by those skilled in the art. The Applicants are claiming the peptide, which may be formed from the nucleic acid. Withdrawal and reconsideration of the rejection is requested.

The Examiner has also rejected claims 3 and 14 stating, "Claims 3 and 14 broaden the base claims 1 and 12, respectively with the recitation of a 'concatemer' of the peptide. Each of the base claims recites only a single peptide." (Official Action at page 4.) Claims 3 and 14 have been amended to advance prosecution. The Examiner's rejection is obviated.

The Examiner has also rejected claim 12 stating, "[It] is indefinite as to the selection of a peptide from a library and does not further limit or adds [sic] any characterization to the peptide

selected therein." (Official Action at page 4.) Claim 12 has been amended to an independent claim to advance prosecution. The Examiner's rejection is obviated.

Rejection of Claims 1-2 and 12-14 under, 35 U.S.C. § 102 (e)

The Examiner has rejected claims 1-2 and 12-14 under 35 U.S.C. § 102 (e) as being anticipated by Wei et al. The Examiner asserts, "Wei discloses a specific peptide sequence that contains the elected species consists only of sequences FEFVG or this sequence comprised other amino acid residues besides the one given therein i.e., embedded in a longer peptide sequence. Accordingly, the specific polypeptide of Wei containing specific residues anticipates the broadly claimed peptides having other undefined amino acid residues in the FEFVG sequence." (Official Action at page 5. (Emphasis in the original)) Applicants respectfully traverse this rejection.

Wei et al. teaches a human MutT2 polypeptide and DNA (RNA) encoding the polypeptide and a procedure for producing the polypeptide recombinantly. (See Abstract.) The polypeptide of Wei et al., or the polynucleotide encoding the polypeptide, can be used to prevent and treat diseases associated with errors in DNA replication. (See col. 2, lines 31-33.) Wei et al. teaches that the polypeptides of its invention includes the polypeptide of SEQ ID NO: 2, which is the deduced amino acid sequence of hMutT2, or biologically active portions thereof containing at least 30 amino acids and preferably 50 amino acids. (See col. 6, lines 25-36, and col. 5, lines 54-58.)

The peptides of the instant invention enhance cell growth, inhibit cell growth, and enhance or inhibit production of cellular proteins. These peptides can be used as substitutes for

hydrolysates that are typically used as supplements in culture media. The peptides of the present invention are not structurally equivalent to polypeptide of Wei et al. The polypeptides of Wei et contain at least 30 amino acids and must have the biological functionality of the full polypeptide. Wei et al. does not teach or suggest peptides, only polypeptides. Wei et al. fails to anticipate the present invention. Applicants requests withdrawal and reconsideration of the rejection.

Rejections of claims 1-3 and 12-14 under 35 U.S.C. 103(a) over Wei et al.

The Examiner has rejected claims 1-3 and 12-14 as being unpatentable over U.S. Patent 6,103,871 by Wei et al. The Examiner asserts, "Wei et al. discloses as peptide sequence as shown in Fig. 2A. The peptide sequence contains the elected species FEFVGF of the hMUTT1. The claimed sequence recites a peptide selected from the different recited peptides sequences one of which is the FEFVG. If the peptide consists only of FEFVG without other residues, then Wei discloses at col. 4, lines 9-17, that fragments of the polypeptide can be made. It would have been obvious to one having ordinary skill in the art at the time the invention was made to delete some of the amino acids in the polypeptide of Wei. One would have been motivated to make a fragment e.g., FEFVG from the longer chain peptide, as commonly done in the art, not only for its easy synthesis but also, because fragment is known to where the activity of a compound resides." (Official Action, page 6.) Applicants respectfully traverse this rejection.

As discussed above, Wei et al. teaches that any portion of the polypeptides must contain at least 30 amino acids and preferably 50 amino acids. (See col. 6, lines 25-36.) Further, any fragment of the polypeptide must retain essentially the same biological function or activity of the

polypeptide. (See col. 5, lines 54-58.) The Examiners assertion of motivation to make the selected fragment of Applicants invention from the larger polypeptide protein of Wei et al. for want of ease and "because fragment is known [that] to where the activity of a compound resides" is hindsight, which is inappropriate.

As stated by the Court of Appeals for the Federal Circuit in the case of *In re Dembiczak*, 50 USPQ2d 1614 (1999):

> A claimed invention is unpatentable if the differences between it and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. Section 103(a) (Supp. 1998); see *Graham v. John Deere Co.*, 383 U.S. 1, 14, 148 USPQ 459, 465 (1966). The ultimate determination of whether an invention is or is not obvious is a legal conclusion based on underlying factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness. See *Graham*, 383 U.S. at 17-18, 148 USPQ at 467; *Miles Labs, Inc., Inc. v. Shandon Inc.*, 997 F.2d 870, 877, 27 USPQ2d 1123, 1128 (Fed. Cir. 1993). ...
>
> Our analysis begins in the text of section 103 quoted above, with the phrase "at the time the invention was made." For it is this phrase that guards against entry into the "tempting but forbidden zone of hindsight," see *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 873, 228 USPQ 90, 98 (Fed. Cir. 1985), overruled on other grounds by *Nobelpharma AB v. Implant Innovations, Inc.*, 141 F.3d 1059, 46 USPQ2d 1097 (Fed. Cir. 1998), when analyzing the patentability of claims pursuant to that section. Measuring a claimed invention against the standard established by section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. See, e.g. , *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 UPSQ 303, 313 (Fed. Cir. 1983). Close adherence to this methodology is especially important in the case of less technologically complex inventions, where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." Id.

> Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., *C.R. Bard, Inc. v. M3 Sys., Inc.* , 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998) (describing "teaching or suggestion or motivation [to combine]" as an "essential evidentiary component of an obviousness holding"); *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) ("the Board must identify specifically . . . the reasons one of ordinary skill in the art would have been motivated to select the references and combine them"); *In re Fritch* , 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (examiner can satisfy burden of obviousness in light of combination "only by showing some objective teaching [leading to the combination]"); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) (evidence of teaching or suggestion "essential" to avoid hindsight); *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 297, 227 USPQ 657, 667 (Fed. Cir. 1985) (district court's conclusion of obviousness was error when it "did not elucidate any factual teachings, suggestions or incentives from this prior art that showed the propriety of combination"). See also *Graham* , 383 U.S. at 18, 148 USPQ at 467 ("strict observance" of factual predicates to obviousness conclusion required). Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability -- the essence of hindsight. See, e.g., *Interconnect Planning Corp. v. Fei* , 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed. Cir. 1985) ("The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time."). In this case, the Board fell into the hindsight trap.

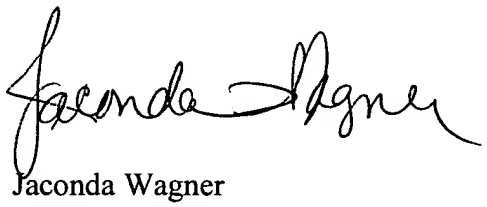
The teachings of Wei et al. do not indicate a functional peptide of less than 20 amino acids. As such, the Examiner's assertion that one skilled in art would have been motivated to make the peptides of the present invention is impermissible hindsight. Withdrawal and reconsideration of the rejection is respectfully requested.

CONCLUSION

Applicants believe the present invention to be novel and unobvious and respectfully request a Notice of Allowance clearly stating the grounds of patentability. However, should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Jaconda Wagner (Reg. No. 42,207) at the telephone number below, to conduct an interview in an effort to expedite prosecution of the present application. Please note that attached hereto is a marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-1666 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,



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Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (amended) The peptide of claim 2 wherein [expression of] the recombinant nucleic acid sequence is expressed so that it produces a concatemer of the peptide which is [cleavable by chemical or enzymatic means] cleaved chemically or enzymatically to release the peptide [monomers].

12. (amended) A peptide selected from [the library of Claim 5] a peptide library comprising chemically synthesized peptides, wherein each of the peptides comprises an N-terminal or C-terminal amino acid associated with enzymatic or chemical cleavage of a polypeptide and one or more additional amino acids.

14. (amended) The peptide of claim 13 wherein [expression] the recombinant nucleic acid sequence is expressed so that it produces a concatemer of the peptide which is [cleavable by chemical or enzymatic means] cleaved chemically or enzymatically to release the peptide [monomers].